REMARKS

Claims 1, 2, 7-12, 14-24 and 27-41 are currently pending in the present application. No amendment has been made.

All previous rejections have been withdrawn. The Examiner has rejected claims 1, 2, 7-12, 14-24 and 27-41 on new ground, i.e., as being unpatentable under 35 U.S.C. § 103(a) over the combined disclosures of U.S. Patent Application Publication No. 2003/0068378 ("the '378 application") in view of U.S. Patent No. 6,099,863 ("the '863 patent") and further in view of U.S. Patent No. 5,904,929 ("the '929 patent"). The '378 application is newly cited in the pending Office Action, and the '863 and '929 patents have been cited previously.

The Examiner states that "it would have been obvious to include the galanthamine salt of the '863 patent into the thin oral films of the '149 patent [*sic*,'378 application] since the '149 [*sic*,'378] reference is suggestive of cholinesterase inhibitors and discloses fast dissolving oral dosage forms." The Examiner continues that the "combination would have been obvious following the suggestions of the '149 [*sic*,'378] application and teachings of the '863 to quickly deliver the compounds orally."

Applicants respectfully submit that claim 1 and its dependent claims are not *prima facie* obvious in view of the combination of the '378 application and the '863 and '929 patents, at least because the cited prior art did not teach to use a film-shaped dosage form that is not mucoadhesive as that recited in claim 1. The purpose of the '378 application is to overcome the problems caused by the mobility of prior art dosage units within the mouth. In particular, the '378 application's dosage units "are not mobile in the mouth because on contact with the moist mucosal surface, the film becomes a coating that adheres to the mucosal surface and then disintegrates and dissolves over a timeframe controlled in the design of the dosage." [para. 24] The '378 application clearly states that upon administration to the subject by being placed on a mucous surface, "the film becomes a mucoadhesive coating." [para. 30] Indeed, a mucosal adhesion enhancer is included in the dosage form to ensure mucoadhesiveness. [See e.g., Abstract, claim 1]

Consequently, the '378 application cannot be used as an appropriate primary reference, because it is directed to a dosage unit that is clearly distinguished from that recited in claim 1. Contrary to the Examiner's position, the '378 application teaches away from the invention

recited in claim 1 and provides no motivation for one skilled in the art to use films that are not mucoadhesive in order to arrive at the subject matter recited in the present claims.

Even assuming the '378 application was an appropriate primary reference, which Applicants strongly disagree, it would not have been obvious to incorporate galanthamine or any of its derivatives into the films of the '378 application or any film dosage form for buccal administration. As discussed in the specification of the present application, side-effects were known to be associated with the oral administration of fast release dosage forms of galanthamine. The skilled artisan would have been discouraged from using a rapid release film-shaped formulation for buccal administration of galanthamine, because such formulation was expected to have a faster onset of action in the oral cavity than the tablets that deliver galanthamine to the gastrointestinal tract. An even higher plasma concentration galanthamine, thus more severe side-effects, would have been expected from the buccal administration of film-shaped formulation for galanthamine. See para. [0019].

The '378 application, as well as the '863 and '929 patents, provided no specific motivation for one skilled in the art to use a rapid release film-shaped formulation for buccal administration of galanthamine or salts or derivatives thereof. The '378 application provides a laundry list of hundreds of actives, which include, in general terms, anti-Parkinson's drugs and anti-Alzheimer drugs. [para. 42]. Contrary to the Examiner's statement, cholinesterase inhibitors are not specifically suggested by the '378 application. In the absence of specific teaching, in view of the known side-effects associated with the fast release oral dosage forms of galanthamine, one skilled in the art would not be motivated to choose galanthamine for delivery with the mucoadhesive film of the '378 application, let alone a film that is not mucoadhesive which the '378 application teaches against.

Furthermore, the combination of the cited references does not teach the dissolution profile recited in the present claims, i.e., within thirty minutes after buccal administration, the medicaments release such an amount of the cholinergic active substance(s) contained therein to the oral cavity that an effective plasma level is achieved. A mucoadhesive film as that described in the '378 application can have very different dissolution profiles compared to that of the presently claimed. The Examiner has not provided any evidence to support his inherency statement.

Only through innovative experimentation, Applicants discovered for the first time that a film-shaped formulation for buccal administration of galanthamine affords rapid onset of action to achieve the effective plasma level without the occurrence of unacceptable peripheral side effects. As discussed in detail in the specification, such superior result is completely unexpected. See e.g., para. [0019]. The superior result is particularly surprising in view of the '378 application, because the reference teaches away from using a film-shaped preparation that is not mucoadhesive.

Accordingly, reconsideration and withdrawal of the rejection of claims 1-3, 7-9, 11, 12, 14-24 and 27-41 for being unpatentable over the combination of the '378 application and the '863 and '929 patents are respectfully requested.

It is respectfully submitted that the present application, including claims 1, 2, 7-12, 14-24 and 27-41, is in condition for allowance and such action is respectfully solicited. Applicants appreciate the effort of the Examiner and look forward to receiving the Notice of Allowance of all pending claims.

Respectfully submitted,

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1/13/2011 (Date) By: _____

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